

Género

Candida

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Candidiasis y las levaduras del género *Candida*

- Candidiasis: infección por hongos más frecuente del territorio BMF, afecta piel y mucosas
- Causada por levaduras unicelulares del género *Candida*

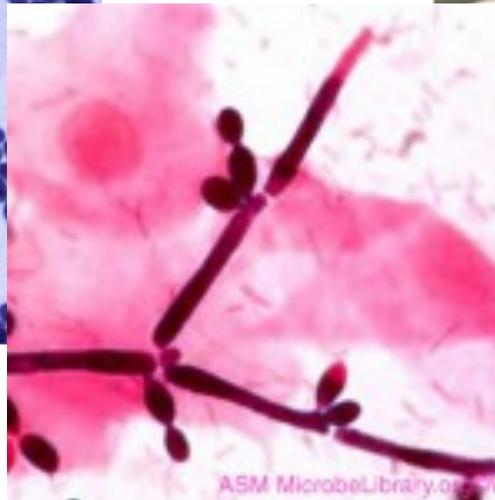
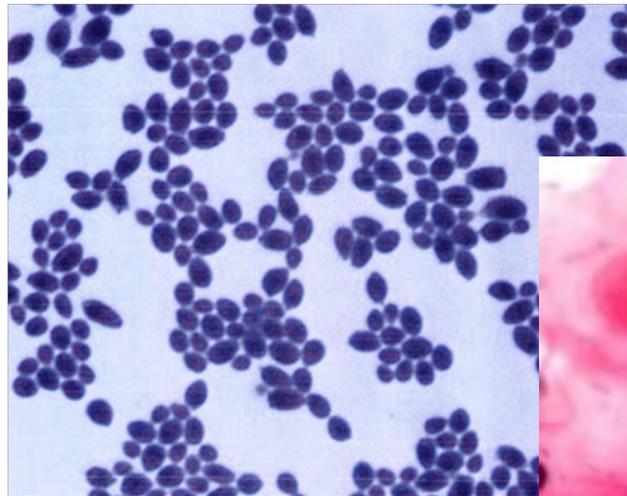


Candida albicans



Levaduras del género *Candida* - ¿ Quiénes son ?

- Hongos unicelulares
- Aspecto microscópico
- Agentes etiológicos de candidiasis BMF y diseminadas (órganos profundos/ sistémicas)



Taxonomía género *Candida*

| Family/genus or clade | Species | Genetic markers |
|--------------------------------------|--|-----------------|
| Debaryomycetaceae | | |
| <i>Lodderomyces/Candida albicans</i> | <u><i>C. albicans</i></u> , <i>C. blackwelliae</i> ^{a,c} , <i>C. bohioensis</i> ^c , <i>C. buenavistaensis</i> , <i>C. chauliodes</i> , <i>C. corydali</i> , <u><i>C. dubliniensis</i></u> , <i>C. frijolesensis</i> , <i>C. gigantensis</i> , <i>C. hyderabadensis</i> ^a , <i>C. jiufengensis</i> ^a , <i>C. labiduridarum</i> , <i>C. maltosa</i> , <u><i>C. metapsilosis</i></u> ^a , <i>C. morakotiae</i> ^a , <i>C. neerlandica</i> , <u><i>C. orthopsilosis</i></u> , <i>C. oxycetoniae</i> ^a , <i>C. parapsilosis</i> , <i>C. prachuapensis</i> ^a , <i>C. pseudojiufengensis</i> ^a , <i>C. sakaeoensis</i> ^a , <i>C. sanyaensis</i> ^a , <i>C. saraburiensis</i> ^a , <i>C. sojiae</i> , <i>C. tetrigidarum</i> , <i>C. theae</i> ^a , <u><i>C. tropicalis</i></u> , <i>C. verbasci</i> , <i>C. viswanathii</i> | SSU, D1/D2 LSU |
| <i>Candida glabrosa</i> clade | <i>C. fluviatilis</i> , <i>C. glabrosa</i> , <i>C. manassasensis</i> , <i>C. palmioleophila</i> , <i>C. pseudoglabrosa</i> , <i>C. saitoana</i> , <i>C. sphagnicola</i> | SSU, D1/D2 LSU |
| <i>Candida kruisii</i> clade | <i>C. aglyptini</i> ^c , <i>C. atbi</i> , <i>C. barrocoloradensis</i> , <i>C. cretensis</i> , <i>C. gatunensis</i> , <u><i>C. kruisii</i></u> , <i>C. lycoperdinae</i> , <i>C. pallodes</i> , <i>C. panamensis</i> , <i>C. stri</i> , <i>C. tritomae</i> | SSU, D1/D2 LSU |
| <i>Candida tanzawaensis</i> clade | <i>C. ambrosiae</i> , <i>C. anneliseae</i> , <i>C. atakaporum</i> , <i>C. bokatorum</i> , <i>C. bolitotheri</i> , <i>C. bibrorum</i> , <i>C. canberraensis</i> , <i>C. chickasaworum</i> , <i>C. choctaworum</i> , <i>C. emberorum</i> , <i>C. guaymorum</i> , <i>C. kunorum</i> , <i>C. maxii</i> , <i>C. panamericana</i> , <i>C. prunicola</i> , <i>C. pyralidae</i> , <i>C. taliae</i> , <i>C. tanzawaensis</i> , <i>C. terraborum</i> , <i>C. vadensis</i> ^a , <i>C. wounanorum</i> , <i>C. xylopsoci</i> , <i>C. yuchorum</i> | SSU, D1/D2 LSU |

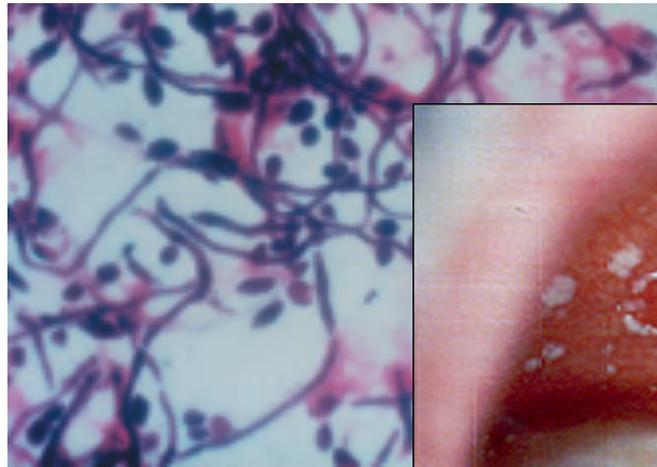
Candida spp.: especies de hongos más frecuentes en la cavidad oral

Candida albicans
corresponde a más del
80% de los aislados de
cultivos de este género

| Table 9.1 Fungal species recovered from the human mouth. | |
|---|--------------------------------------|
| <i>Candida</i> species | Other fungal species (rare) |
| <i>Candida albicans</i> | <i>Paracoccidioides brasiliensis</i> |
| <i>Candida glabrata</i> | <i>Aspergillus</i> spp. |
| <i>Candida tropicalis</i> | <i>Cryptococcus neoformans</i> |
| <i>Candida krusei</i> | <i>Histoplasma capsulatum</i> |
| <i>Candida lusitaniae</i> | <i>Mucor</i> spp. |
| <i>Candida dubliniensis</i> | <i>Saccharomyces</i> spp. |
| <i>Candida kefyr</i> | <i>Geotrichum</i> spp. |
| <i>Candida guilliermondii</i> | <i>Rhizopus</i> spp. |
| <i>Candida parapsilosis</i> | |

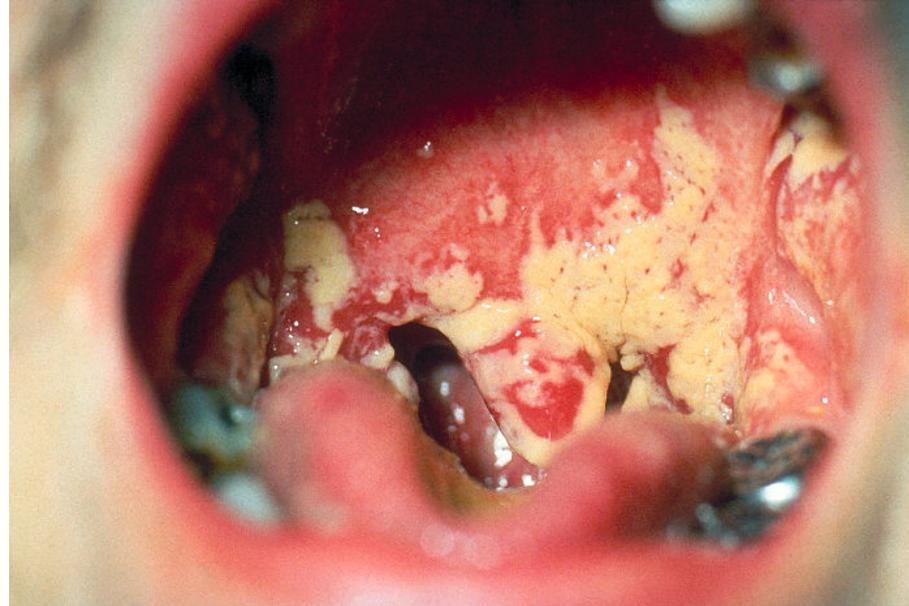
Levaduras del género *Candida* - Hábitat

- Parte de la microbiota comensal
- Colonizan asintómicamente piel y mucosas
- Hasta un 60% de los adultos sanos presenta *C. albicans* en la cavidad oral y un 26-65% de los niños sanos

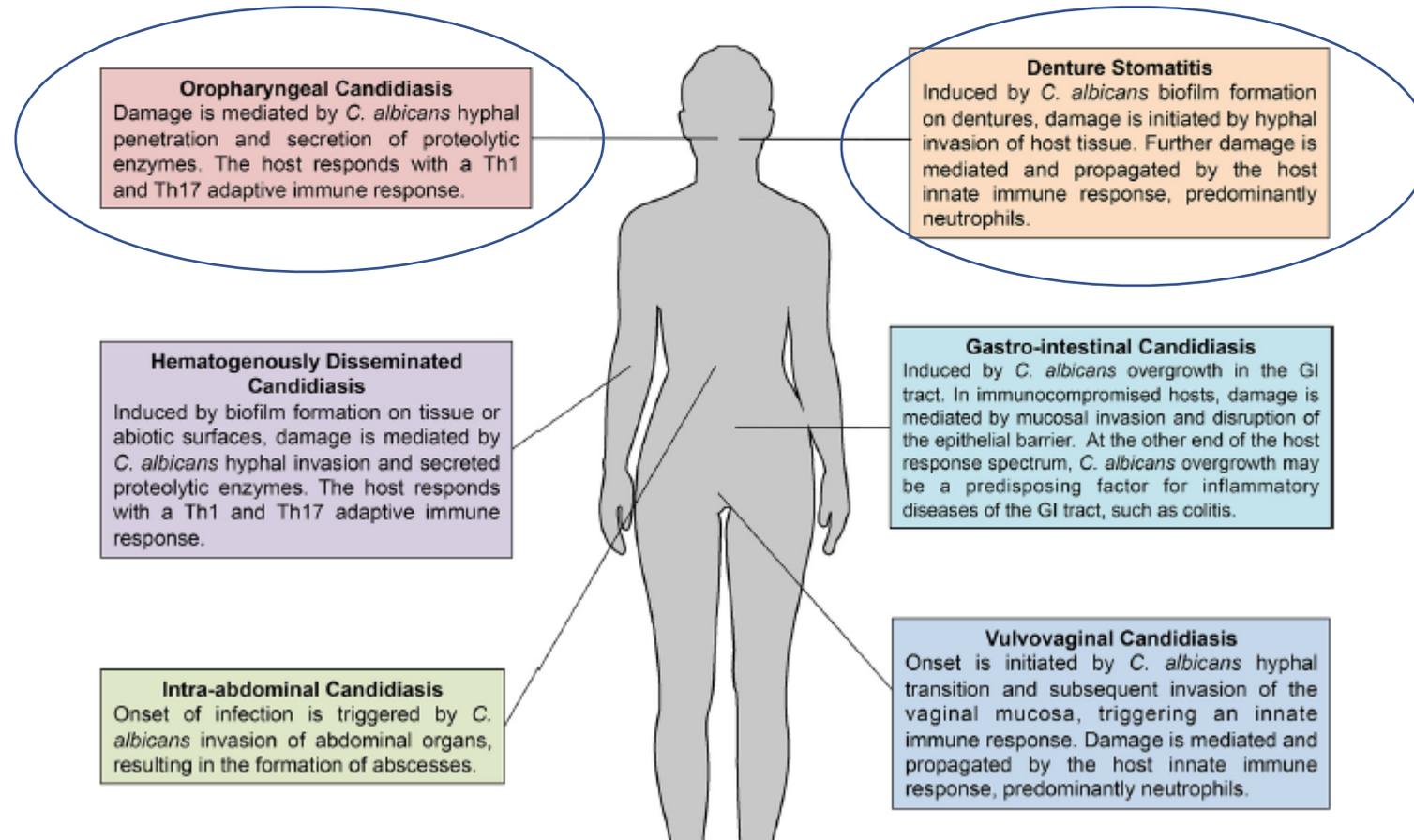


Levaduras del género *Candida* - Importancia

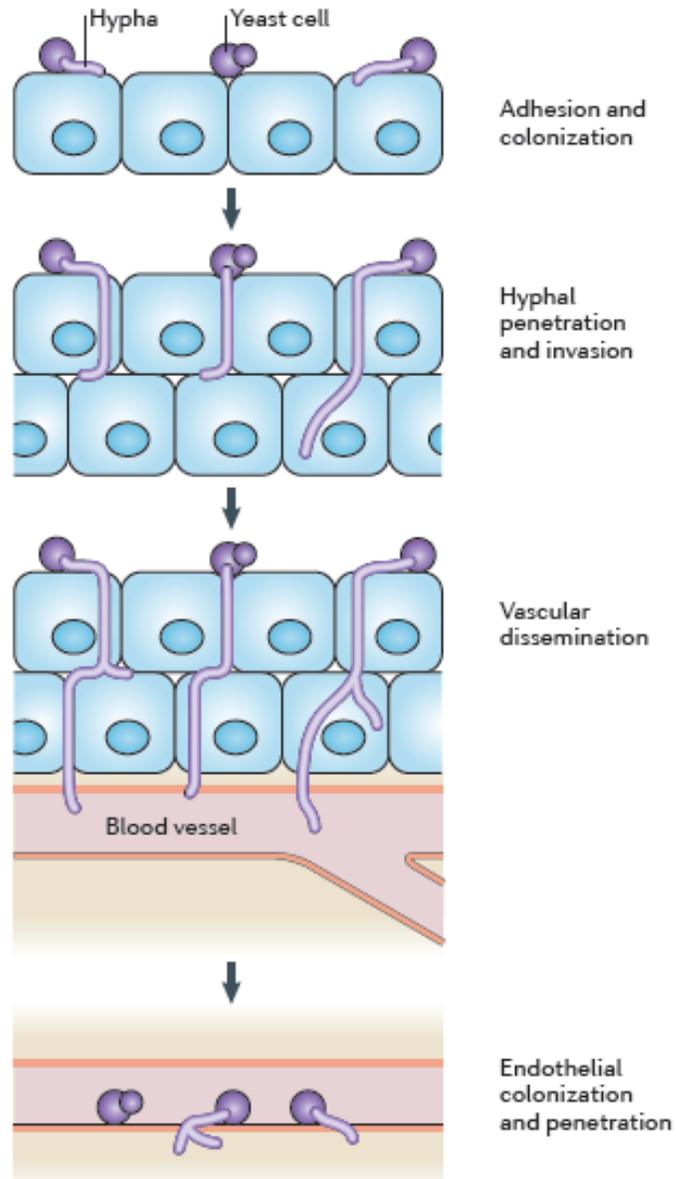
- Candidiasis – infección micótica oportunista más frecuente en el hospedero humano
- Factores propios del hospedero son determinantes
- Es el principal agente de infecciones nosocomiales



Cambio de estado de salud y enfermedad asociado a *Candida*



Diseminación hematológica de levaduras del género *Candida*



- Causan infecciones sistémicas en pacientes debilitados .
- Tercera causa de infecciones del torrente sanguíneo en UCI con alta mortalidad 35- 60%
- La especie aislada con mayor frecuencia es *albicans*, pero han emergido otras especies
- Se ha observado un cambio epidemiológico entre la especie *albicans* y otras junto a su patrón de susceptibilidad

**TABLE
6-1**

Clinical Forms of Oral Candidiasis

| Clinical Type | Appearance and Symptoms | Common Sites | Associated Factors and Comments |
|---|--|--|--|
| Pseudomembranous (thrush) | Creamy-white plaques, removable; burning sensation, foul taste | Buccal mucosa, tongue, palate | Antibiotic therapy, immunosuppression |
| Erythematous | Red macules, burning sensation | Posterior hard palate, buccal mucosa, dorsal tongue | Antibiotic therapy, xerostomia, immunosuppression, idiopathic |
| Central papillary atrophy (median rhomboid glossitis) | Red, atrophic mucosal areas; asymptomatic | Midline posterior dorsal tongue | Idiopathic, immunosuppression |
| Chronic multifocal | Red areas, often with removable white plaques; burning sensation, asymptomatic | Posterior palate, posterior dorsal tongue, angles of mouth | Immunosuppression, idiopathic |
| Angular cheilitis | Red, fissured lesions; irritated, raw feeling | Angles of mouth | Idiopathic, immunosuppression, loss of vertical dimension |
| Denture stomatitis (chronic atrophic candidiasis, denture sore mouth) | Red, asymptomatic | Confined to palatal denture-bearing mucosa | Probably not true infection; denture often is positive on culture but mucosa is not |
| Hyperplastic (candidal leukoplakia) | White plaques that are not removable; asymptomatic | Anterior buccal mucosa | Idiopathic, immunosuppression; care must be taken not to confuse this with other keratotic lesions with superimposed candidiasis |
| Mucocutaneous | White plaques, some of which may be removable; red areas | Tongue, buccal mucosa, palate | Rare; inherited or sporadic idiopathic immune dysfunction |
| Endocrine-candidiasis syndromes | White plaques, most of which are not removable | Tongue, buccal mucosa, palate | Rare; endocrine disorder develops after candidiasis |

- Formas clínicas variadas de Candidiasis Oral
- Micosis superficiales de tipo oportunista

Factores asociados al desarrollo de Candidiasis oral

| Sistémicos | |
|---|--|
| Edades extremas | |
| Condiciones que generan inmuno-compromiso | |
| Enfermedades metabólicas (diabetes) | |
| Infecciones concurrentes | Locales |
| Terapias con antibacterianos | Uso prolongado de corticoides (orales y/o inhaladores) |
| Radioterapia | Hipofunción de glándulas salivales |
| | Flujo salival disminuído |
| | Dieta rica en carbohidratos |
| | Fumar |

Pacientes susceptibles a desarrollar Candidiasis oral

- Personas mayores
- Particularmente aquellas institucionalizadas y portadoras de prótesis removible



Cambios en el ecosistema oral asociados al envejecimiento

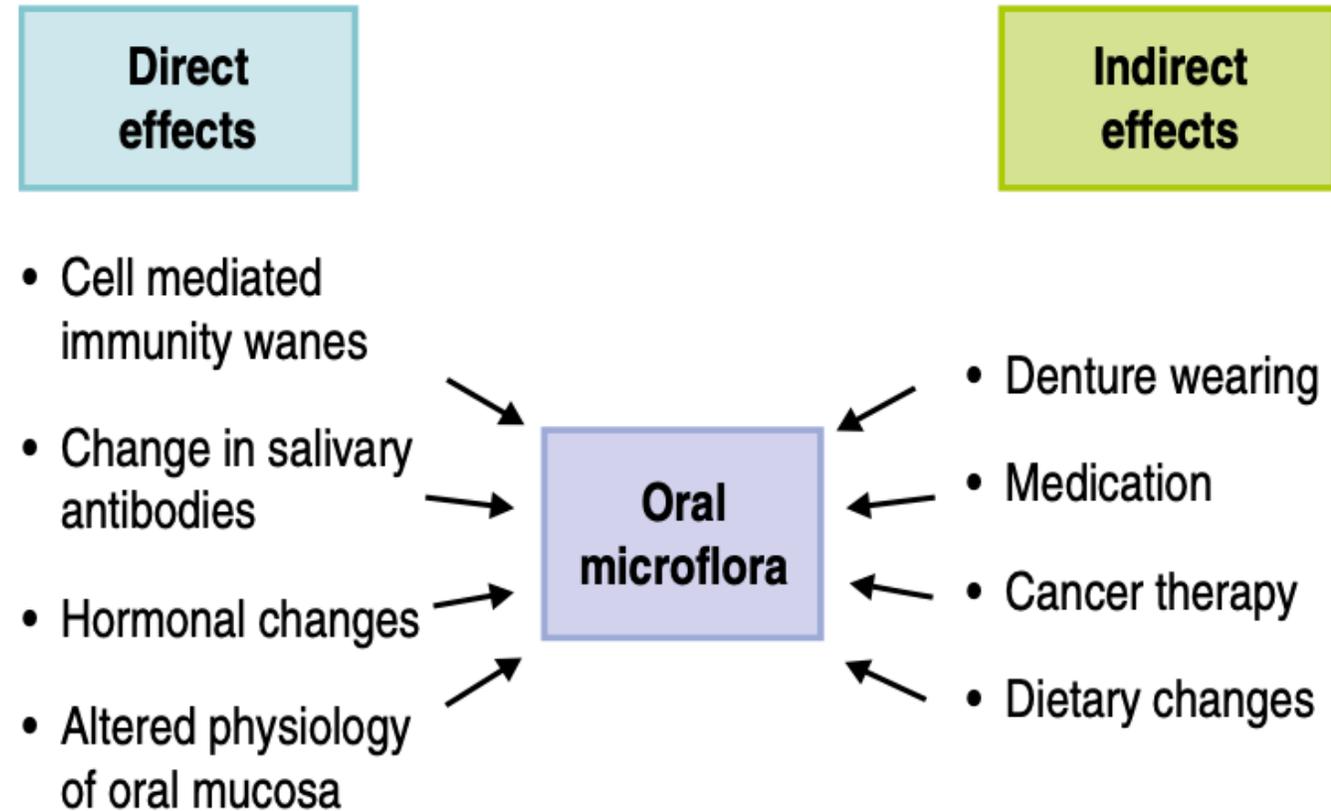


Fig. 4.3 Direct and indirect effects of ageing on the oral microflora.

C. albicans especie recuperada con mayor frecuencia en Candidiasis Oral

- Consenso en la literatura que en diversas poblaciones *C. albicans* es la especie recuperada con mayor frecuencia de estas infecciones

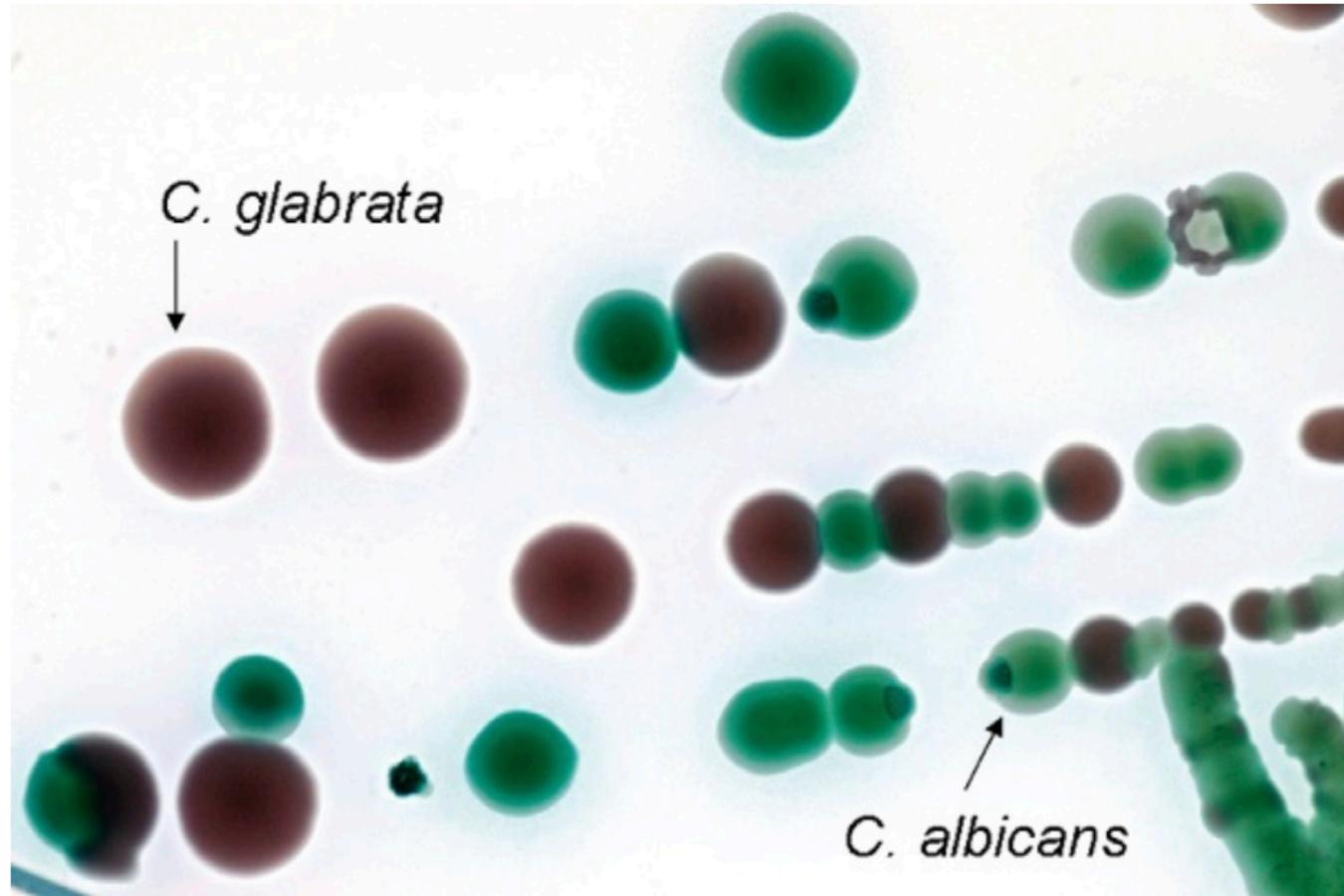
Results: In total, 9769 (6.09%) of the 160,357 patients screened were diagnosed with oral candidiasis on the basis of both clinical manifestations and laboratory testing. The ratio of females to males was 1:0.61, and females had higher overall infection rates than males in all age subgroups. Patients with HIV infection, anaemia-related stomatitis, Sjögren's syndrome/xerostomia, pemphigoid, and radiation-induced stomatitis were highly susceptible to oral candidiasis. Of the 11,161 isolated *Candida* strains, *C. albicans* remained the most common species (75.37%), followed by *C. tropicalis* (6.06%), *C. krusei* (2.79%), and *C. glabrata* (2.02%). Surprisingly, both the proportion and the number of *C. glabrata* isolates increased dramatically over the 4 consecutive years.

Técnicas para el diagnóstico de levaduras del género *Candida*

Table 9.4 Methods of recovering *Candida* from the oral cavity.

| Isolation method | Advantages | Disadvantages |
|-------------------------|---|---|
| Culture of whole saliva | Sensitive; viable organisms isolated | Problems may occur with collection of sample; not site specific |
| Concentrated oral rinse | Quantitative; viable cells isolated | Some patients have difficulty in using rinse; not site specific |
| Swab | Simple to use; viable cells isolated; site specific | Difficult to standardise |
| Smear | Simple to use; not reliant on culture | Viable cells not determined; species identity not readily confirmed |
| Imprint culture | Quantitative; viable cells isolated; site specific | Some sites difficult to sample |
| Biopsy | Essential for chronic hyperplastic candidosis | Invasive; not appropriate for other forms of candidosis |

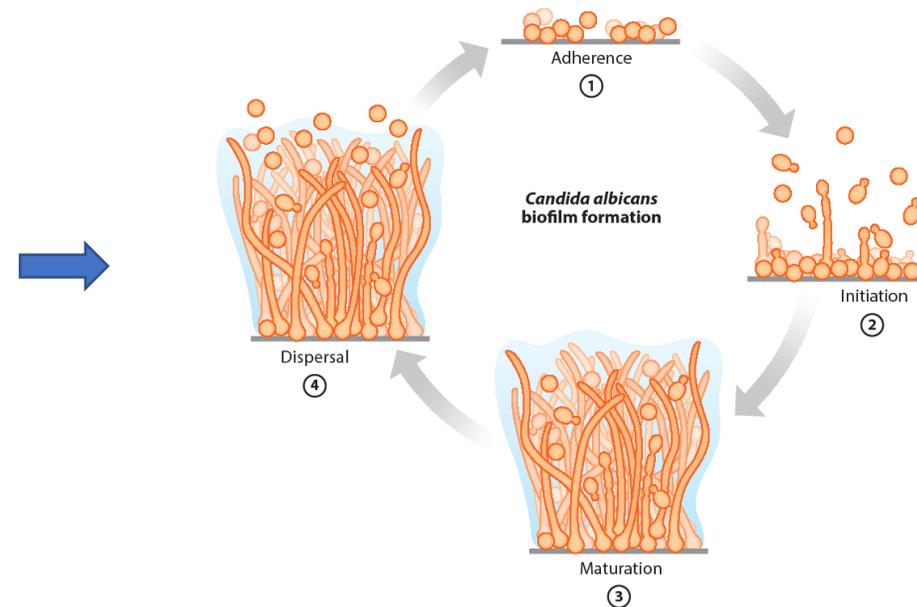
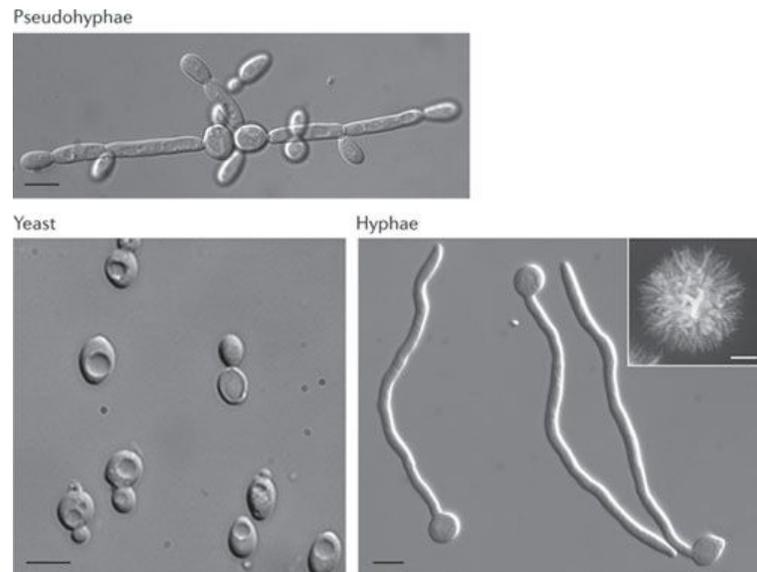
Técnicas para el diagnóstico de levaduras del género *Candida*



CHROMagar *Candida*

¿ Qué determina el cambio del comensalismo a parasitismo ?

- Cambios en el medioambiente oral en el hospedero (locales/sistémicos), disminuyen los mecanismos de inmunológicos de vigilancia y control
- *Candida albicans* genera su transición fenotípica, gatillando cambio de estado de **comensal** a **patogénico**
- Formación de biopelículas es clave, junto con otros mecanismos de patogenicidad



Estructuración de biopelículas de *C. albicans*

a

Oral cavity
C. albicans interacts with:
 • *Staphylococcus aureus*
 • *Streptococcus* spp. (*S. mutans*, *S. salivaris*, *S. gordonii*)
 • *Porphyromonas gingivalis*
 • *Aggregatibacter actinomycetemcomitans*
 • *Acinetobacter baumannii*

Lungs
C. albicans interacts with:
 • *Pseudomonas aeruginosa*
 • *Burkholderia cenocepacia*
 • *Mycobacterium tuberculosis*

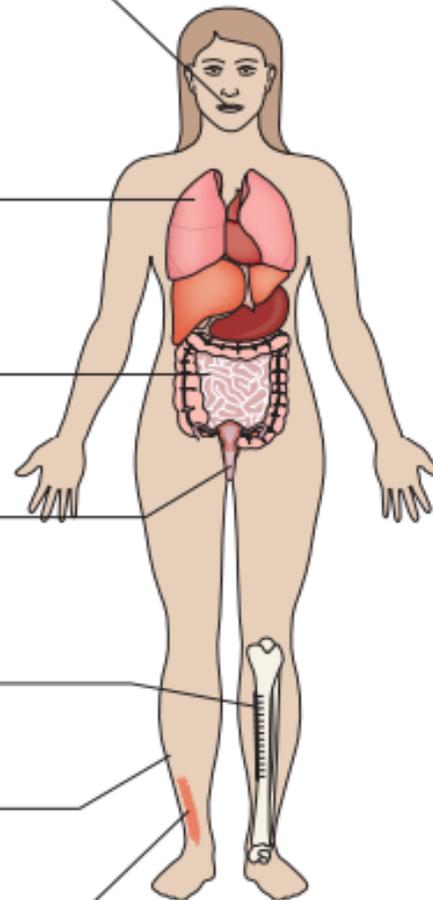
Gastrointestinal tract
C. albicans interacts with:
 • *Escherichia coli*
 • *Helicobacter pylori*
 • *Enterococcus faecalis*
 • *Salmonella* spp.

Vulvovaginal
C. albicans interacts with:
 • *Lactobacillus* spp.

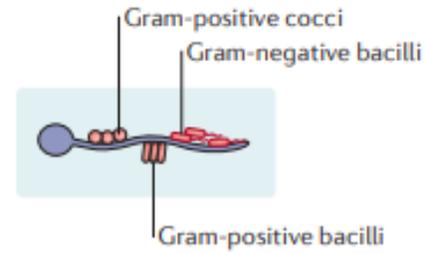
Implanted medical devices
C. albicans interacts with:
 • *S. aureus* • *E. coli*
 • *P. aeruginosa* • *Staphylococcus epidermidis*
 • *E. faecalis* • *epidermidis*

Skin
C. albicans interacts with:
 • *S. aureus*
 • *S. epidermidis*

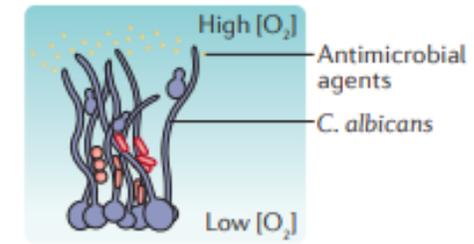
Skin (burn wound)
C. albicans interacts with:
 • *P. aeruginosa*
 • *S. aureus*



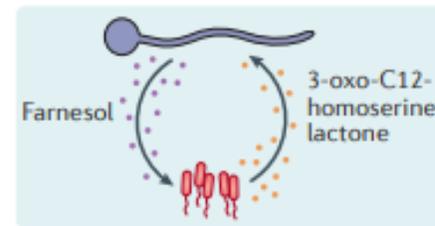
b Physical interactions



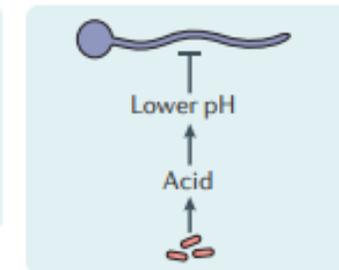
c Synergistic relationship



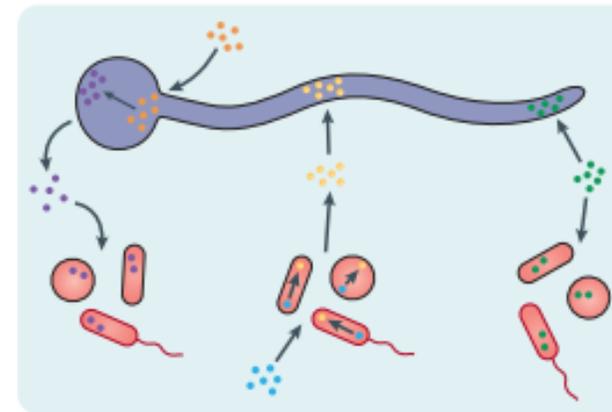
d Signalling



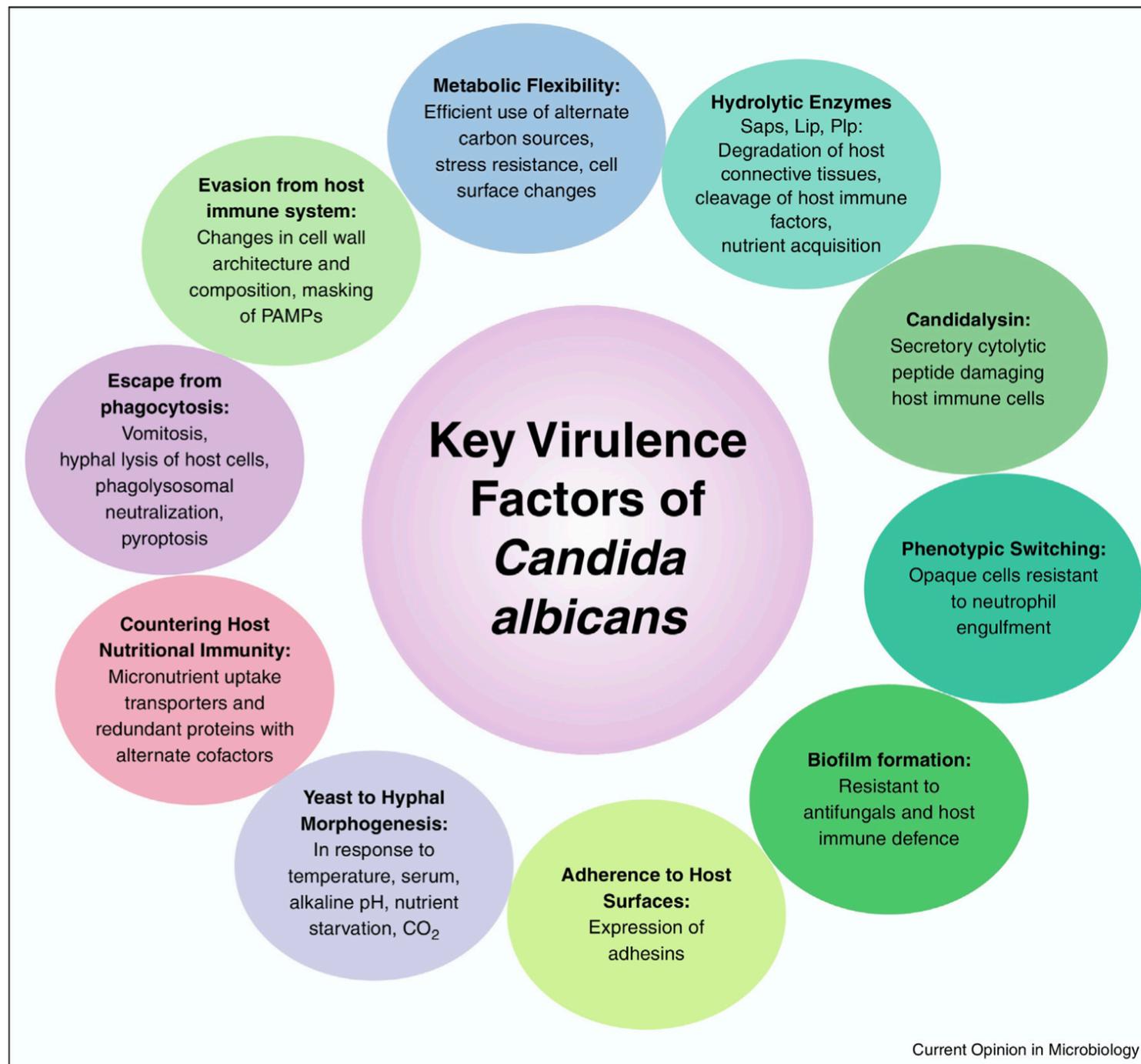
e Antagonistic relationship



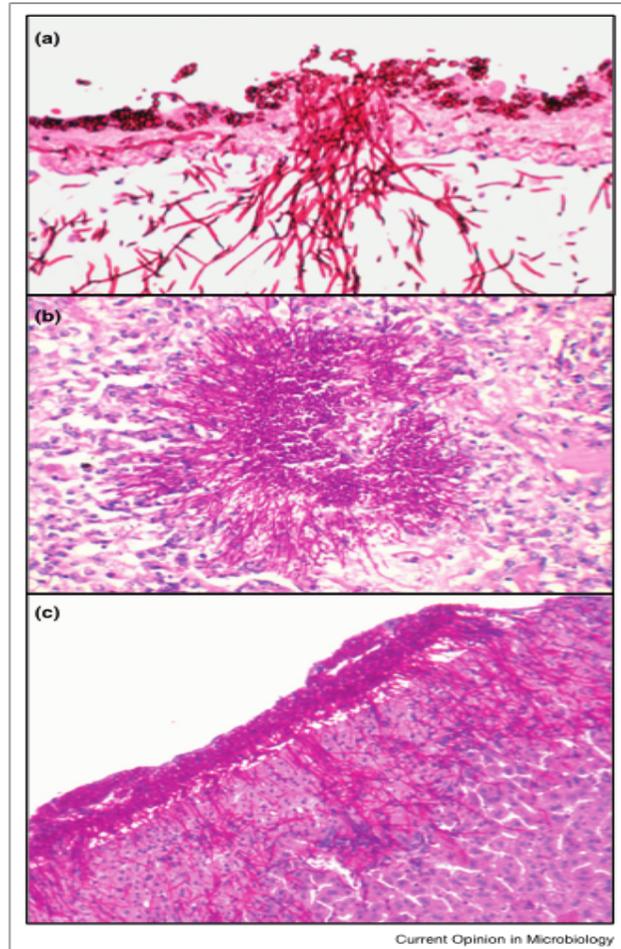
f Nutrient exchange



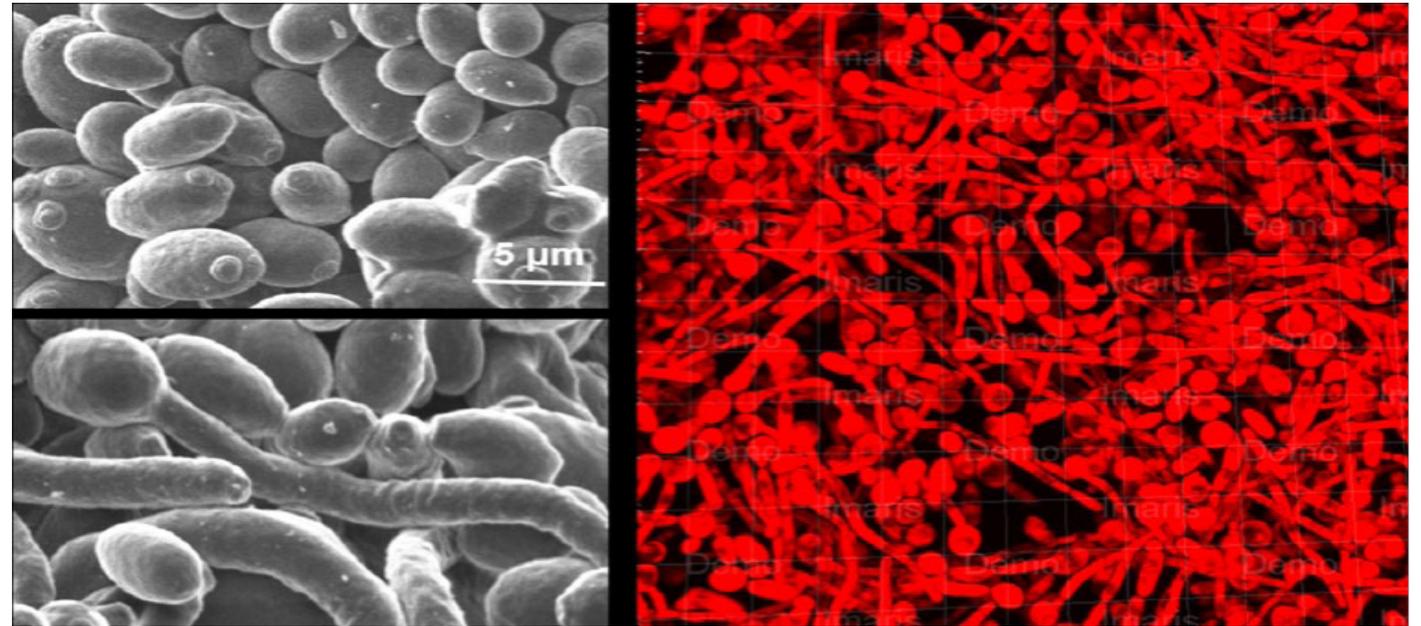
Factores de virulencia de *C. albicans*



Transición fenotípica de *C. albicans*



TOMADO DE:Gow & Hube, Current Opinion in Microbiology 2012



TOMADO DE :Journal of Oral Microbiology 2013. 5: 1-8

Transición fenotípica: Hifas penetran los tejidos del hospedero, se secretan enzimas.

Resistencia a anti-fúngicos



WHAT YOU NEED TO KNOW

- Only three classes of antifungal drugs are available to treat severe *Candida* infections: azoles, echinocandins, and amphotericin B.
- *Candida* species commonly cause bloodstream infections in hospitalized patients. About one in four of these patients die.
- *Candida* species also cause common yeast infections, which can affect the mouth, skin, and vagina, resulting in more than 3.6 million U.S. healthcare visits each year, and \$3 billion estimated direct medical costs.
- Antibiotics used to treat bacterial infections increase the risk of *Candida* infections.

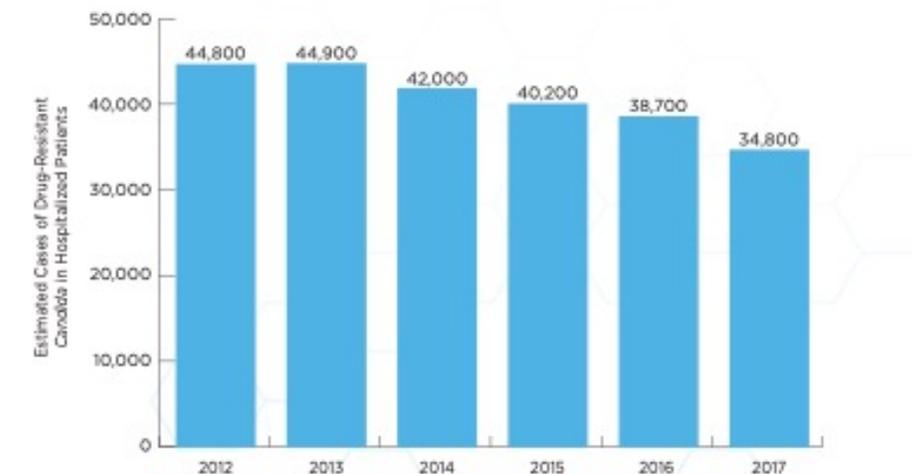
All data represented excludes *C. auris*.



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CASES OVER TIME

Resistant *Candida* are commonly detected in hospitalized patients. About 7% of bloodstream infections are resistant to antifungals.



DRUG-RESISTANT **CANDIDA SPECIES**

THREAT LEVEL **SERIOUS**



34,800

Estimated cases
in hospitalized
patients in 2017

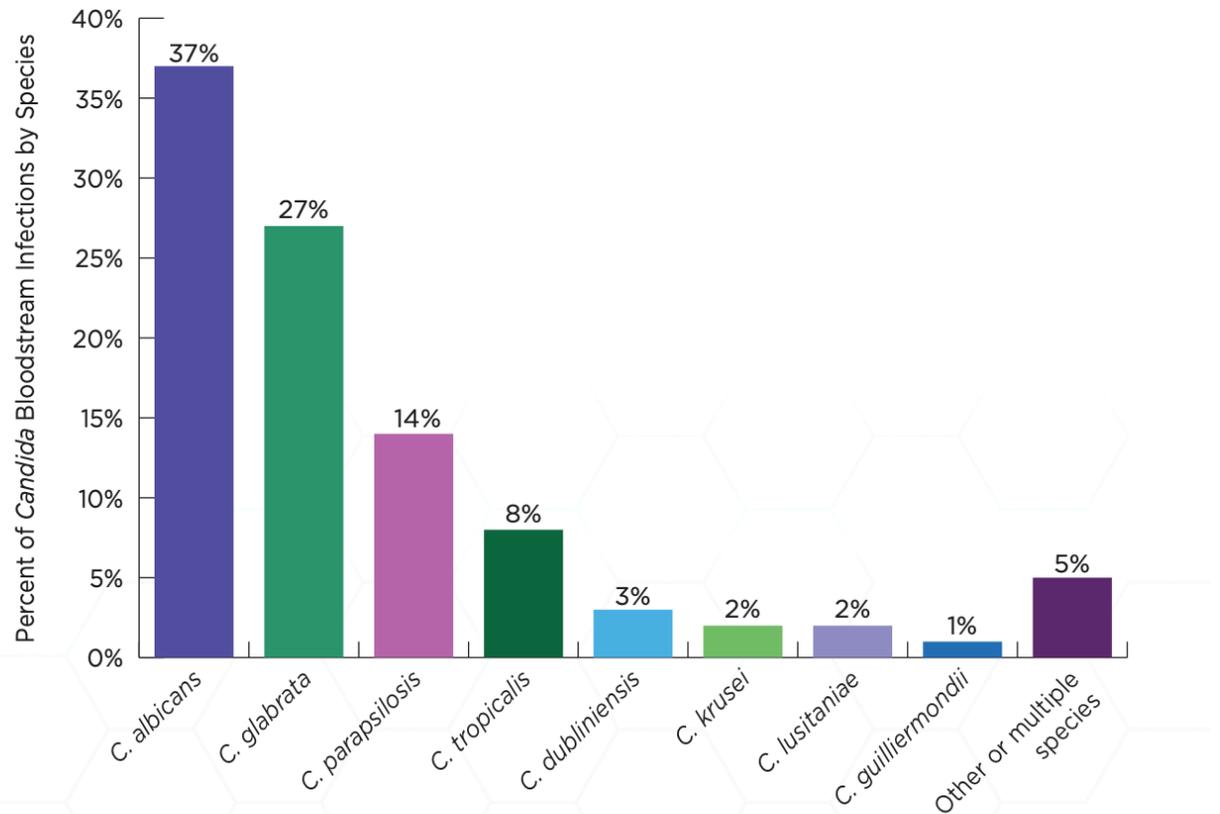


1,700

Estimated
deaths in
2017

BLOODSTREAM INFECTIONS

Candida species are a common cause of bloodstream infections and can be drug-resistant and difficult to treat.



DRUG-RESISTANT **CANDIDA AURIS**

THREAT LEVEL **URGENT**



323

Clinical cases
in 2018

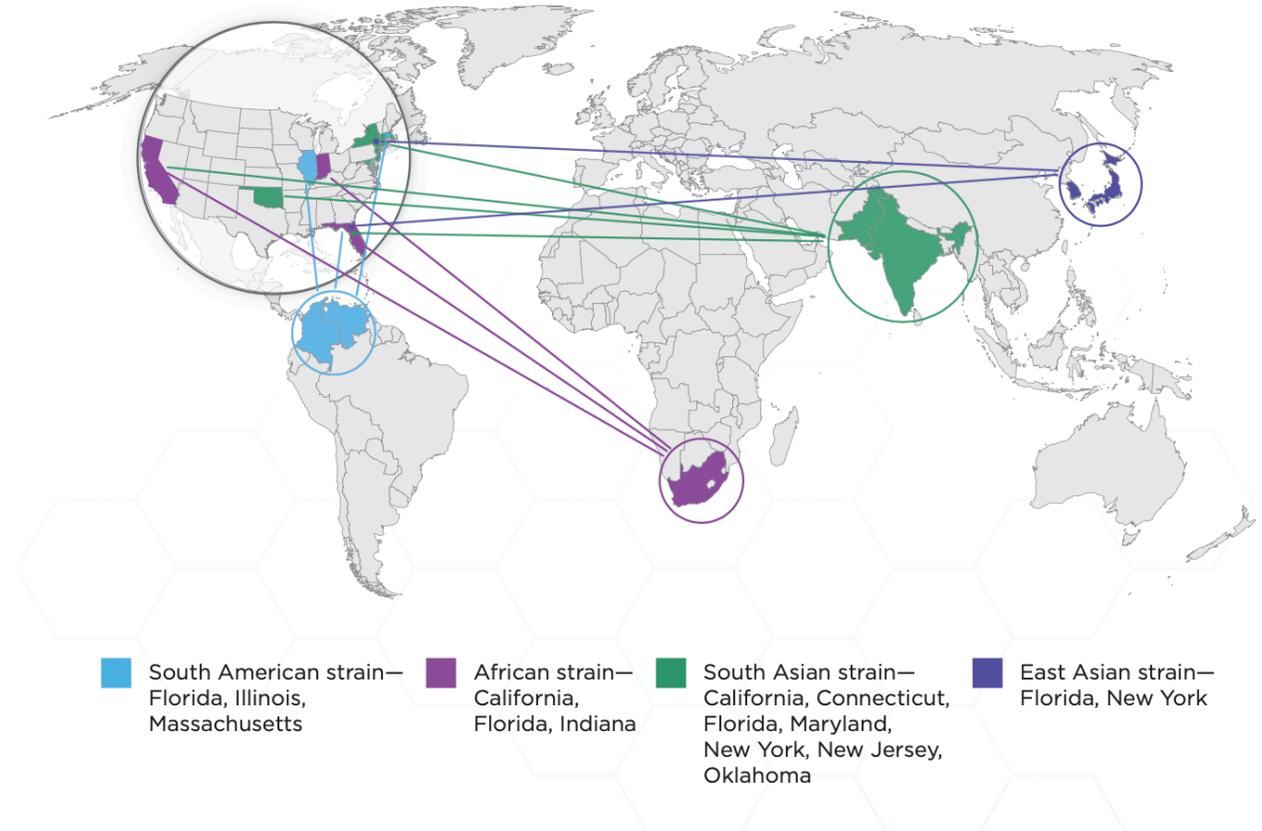


90% Isolates resistant to at least **one** antifungal

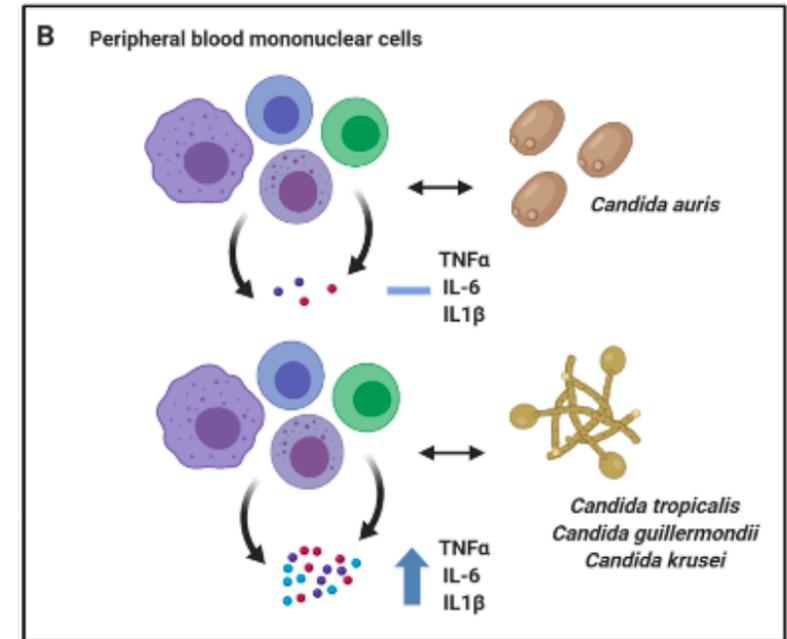
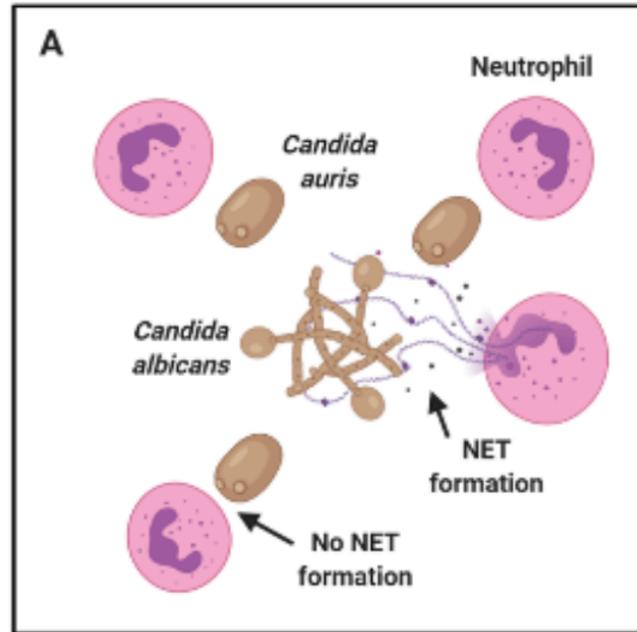
30% Isolates resistant to at least **two** antifungals

A GLOBAL THREAT

Investigators still do not know why four different strains of *C. auris* emerged around the same time across the globe. All four strains have been found in the United States, likely introduced through international travel and subsequent spread in U.S. healthcare facilities.



Evasi3n diferencial del sistema inmune por parte de *Candida auris*





Fin de la clase